**Nelson, Bettie L**

**From:** Walk, Roger A.
**Sent:** Thursday, July 27, 2000 3:27 PM
**To:** Tricker, Anthony; Haussmann, Hans J.; Nelson, Bettie L; Patskan, George J.; Solana, Rick P.; Roemer, Ewald; 'walnutgrove@dellnet.com'; 'islesail@rivnet.net'
**Cc:** Kinser, Robin D.; Sanders, Edward
**Subject:** RE: Total Exposure - Pilot study design

Dear Tony,

Here some quick clarifications and comments in response to your remarks:

- At least Ted and I think that any attendance at the Chicago conference requires very careful thinking on our side. Please check with Ted about our thoughts on this. We do plan for August 3./4., but I have not received the response re availability from all potential participants.
- The pilot study does not have any demographic stratification except male/female.
- We fully agree on the validation issue. But first we must have the suggestions from the CROs before we can analyze them and consider a process to ensure quality and reliability of assay results. We have already discussed potential strategies to address problems in establishing the assays.
- We have already collected criteria for the validation, we would require from any CRO (based on those used to establish assays at ITRI and Batelle). If you have suggestions for such criteria, please let us know.
- The design that was send to the 3 CRO candidates on July 17. It is posted in the Shared Folder under "News". A presentation of this design (pilot + main TES) as presented to the Dept. of Health in Massachusetts 2 days ago is posted in the Shared Folder under "WSA Presentations".
- Re your concerns about the time required for processing the samples: I understand your concern and you may be absolutely right. I would suggest, however' that we wait for the CROs to respond and then work out a way how resources can be enlarged or the design modified or the timeline revisited.

Thank you for your concerns regarding such an important new type of project and your constructive suggestions.
Roger

----Original Message----
**From:** Tricker, Anthony
**Sent:** Thursday, July 27, 2000 11:46 AM
**To:** Walk, Roger A.; Haussmann, Hans J.; Nelson, Bettie L; Patskan, George J.; Solana, Rick P.; Roemer, Ewald; 'walnutgrove@dellnet.com'; 'islesail@rivnet.net'
**Cc:** Kinser, Robin D.; Sanders, Edward
**Subject:** RE: Total Exposure - Pilot study design

Dear All,

I would prefer the first suggested date of 3-4 August. The second date clashes with the 11th International Conference on Smoking or Health (6-10 August in Chicago) which contains several interesting scientific sessions relevant to Company interests including the total exposure study and harm reduction. If the total exposure meeting could take place next week in Richmond, it would also allow coverage of the above conference.

I am concerned that we still have several technical issues which need to be resolved and that each of the suggested biomarkers of exposure and, more importantly, biomarkers of effect, require further detailed discussion.

From an analytical perspective, I do not think that any CRO without prior experience of determining hemoglobin adducts of aromatic amines or NNK metabolites in urine could start from scratch and have a validated analytical method established within 2 months (even if published methods were followed step for step). Until the robustness of the analysis is first validated by the CRO using samples not included in the TES, there is no point in starting the TES. What criteria do we use to judge whether the methods have been suitably validated?

Can we be sure that a demographically representative population can be formed using 60 subjects per group? More importantly, do we actually need a demographically representative population if we are focusing on determining intra- and inter-personal differences? Does the pilot study have the right design to achieve these objectives - I don't think it does.





Source: https://www.industrydocuments.ucsf.edu/docs/mfnj0001

Another major concern I have is the timeframe of the proposed study. Assuming that the pilot study (and I still have not seen the proposal sent to the CROs) still intends to collect 24 h urine samples on 3 different occasions from 120 subjects (60 nonsmokers and 60 smokers), it is totally unrealistic to expect completion of the biomarker analysis by the end of 2000. Based on the current status of the project, I would not even anticipate completion of the pilot study by the end of 2001.

In summary, I think that the only way to resolve the outstanding issues (which are not limited to the above) is in a face-to-face meeting which should take place at the first possible opportunity.

Tony

Original Message-----

**From:** **Walk, Roger A.**
**Sent:** 26 juillet 2000 18:47
**To:** Haussmann, Hans J.; Nelson, Bettie L; Patskan, George J.; Solana, Rick P.; Tricker, Anthony; Roemer, Ewald; walnutgrove@dellnet.com; islesail@rivnet.net
**Cc:** Kinser, Robin D.
**Subject:** FW: Total Exposure - Pilot study design

Dear All,
Dear All,

Richard and Tony are suggesting a 2-day face-to-face meeting to resolve open issues of the design of the pilot total exposure study.

It looks to me that a 2-day meeting in Richmond will not be easy to arrange given the commitments most of us have already in place for the next days. However let's try and let me know your availability for such a meeting (1.5 days) in Richmond for the period August 3,4 and 7,8. At that time we would be able to review the responses from all 3 CRO candidates to our RFP, which is due on August 2,2000. I will distribute all input from the CRO's on the pilot study protocol.

Yesterday the current design was presented to a number of public health representatives and their scientific consultants in Boston. Except for some minor suggestions for potential improvements they expressed their opinion that our ambitious design is scientifically solid and likely to answer the scientific questions that need to be addressed.

Richard and Tony: what are the technical and conceptual issues that, in your opinion, should be resolved? Is there another productive way to do this, in case we cannot organize such a meeting within the timeframe for selecting the CRO and defining the study protocol. Please bear in mind that the practical deadline for a final protocol is Labor Day for the completion of the pilot in the year 2000.

Tony, in case we plan to meet here in Richmond, you might plan to join us for the site-visit at the CROs which will take place during early August.

Thanks for the recommendations.
Roger

----Original Message----
**From:** Tricker, Anthony
**Sent:** Wednesday, July 26, 2000 10:16 AM
**To:** Carchman, Richard; Walk, Roger A.
**Cc:** Solana, Rick P.
**Subject:** RE: Total Exposure

Dear All,
I fully support Richards idea to have a 2-day face-to-face meeting on the TE project to resolve several conceptual and technical issues. Based on the exchange of email with Parexel, in particular the questions raised and suggestions made by the latter, I don't think we are sufficiently prepared to go out and discuss the current study proposal and related technical issues with potential CRO's.





Source: https://www.industrydocuments.ucsf.edu/docs/mfnj0001